Clinical Techniques in
Equine
Practice

Differences in Wound Healing between Horses and Ponies: Application of Research Results to the Clinical Approach of Equine Wounds

Jacintha M. Wilmink, DVM, PhD,* and P. René van Weeren, DVM, PhD, Diplomate ECVS†

Differences in wound healing between horses and ponies have provided valuable information about the intrinsic process of wound healing and the complications that are relatively frequently encountered in the equine. Primary intention healing in ponies is less often complicated by wound dehiscence and bone sequestrum formation compared with horses. Second intention healing is faster in ponies than horses due to a stronger initial inflammatory response and greater contribution of wound contraction to wound closure. These differences can to a large extent be explained by differences in the local inflammatory response, which in turn are caused by differences in the functional capacity of the leukocytes. The wound healing process can be divided into several overlapping phases representing the events occurring during healing (eg, the inflammatory phase, formation of granulation tissue, wound contraction and epithelialization) This paper describes the differences between horses and ponies during these phases and reflects the research results on the treatment of equine wounds. Research has resulted in the perception that in clinical practice a maximal effect of treatment will be obtained if a differential approach is chosen, optimizing conditions for each successive phase of the wound healing process.
Clin Tech Equine Pract 3:123-133

KEYWORDS **primary intention healing, second intention healing, wound healing, wound contraction, ponies, horses**

Horses frequently suffer traumatic wounds and healing of these wounds is often delayed and complicated compared with other species. Although primary or delayed wound closure is the preferred approach to treatment, many cases present with excessive tissue loss and contamination and/or severe vascular compromise making second-intention healing the only option.[1] Second-intention healing is often protracted and complications, such as wound infection, the formation of exuberant granulation tissue and hypertrophic scars, are frequent. These complications are most common in limb wounds, whereas extensive body wounds heal relatively well.[2,3] Delayed and complicated wound healing leads to significant wastage as a considerable number of horses cannot continue their athletic career because of persisting lameness, swollen limbs and extensive scars.

Recent research has revealed differences in wound healing between horses and ponies.[4-6] The results of these studies have provided important insight into the basic processes of wound healing seen in horses and ponies and the common complications seen in horses. As the basic knowledge of the phases of the wound healing process increased, it became obvious that treatment approaches should take into consideration each individual phase and the essential differences between these phases to optimize the outcome. Therefore, veterinarians should have a workable knowledge of the events occurring during wound healing, the factors that may influence these events, and the effects of treatment to optimize wound repair.

Differences in Wound Healing between Horses and Ponies

Primary Intention Healing

Primary closure of traumatic wounds is preferred because healing is usually faster and the cosmetic results are better than after second-intention healing. Unfortunately, primary closure may result in either partial or complete dehiscence of the wound. Whether a wound undergoes dehiscence or not depends on many factors including individual animal-related factors, the wound itself, environmental factors and methods of treatment.[1,7] Infection appears to be the main cause for

*Woumarec, Wageningen.
†Department of Equine Sciences, Faculty of Veterinary Medicine, University of Utrecht, Utrecht.
Address reprint requests to: Jacintha M. Wilmink, Woumarec, Hamsterlaan 4, 6705 CT Wageningen, The Netherlands. E-mail: j.m.wilmink@tiscalimail.nl

1534-7516/04/$-see front matter
doi:10.1053/j.ctep.2004.08.011

Table 1 Success Rate of Primary Closure of Traumatic Wounds in Horses and Ponies, and the Formation of a Sequestrum when Exposed Bone Was Present (* $P < 0.05$)

	Horses (422)	Ponies (89)	Horses %	Ponies %
Euthanasia	85	22	20	25
Treatment:	337	67	80	75
Other than primary closure	120	26	36	39
Primary closure:	217	41	64	61
Successful	53*	16*	24	39
Dehiscence	151	23	70	56
Unknown	13	2	6	5
Exposed bone	105	23		
Sequestrum	33*	1*	31	4
No sequestrum	72	22	69	96

wound dehiscence, although other factors such as tension on the wound margins and excessive movement of the sutured region also play a roll. Healing of a wound is also somewhat dependent on what structures are involved. Damage to the periosteal layer and exposure of the cortical bone can lead to the formation of a bone sequestrum and complicate healing. Apparently bone sequestrum occurs only if exposure is followed by infection of the cortical bone.[8] Therefore, wound infection affects primary closure either by causing wound dehiscence and the formation of a bone sequestrum.

Factors that may influence the chances of wound infection include the elapsed time from injury, the degree of contamination, the degree of tissue damage, and the thoroughness of wound debridement and lavage which appear to be the most important.[1,7] The number of bacteria left after surgical debridement is critical, in combination with factors in the environment that facilitate colonization, such as dead space and devitalized tissue.

Although bacterial colonization and development of infection are greatly influenced by the administration of antibiotics, the effectiveness of the inflammatory response is as least as important for the prevention of infection.[9,10]

All above-mentioned factors related to wound infection have been evaluated in relation to the success rate of healing under clinical circumstances and compared between horses and ponies in a retrospective study.[6] The records of over 500 equine patients with traumatic wounds admitted to a referral clinic were used for this retrospective study. Patients were divided into horses and ponies dependent on the average adult wither height of the breed. The ponies were defined as <1.48 m, the others as horses. The treated ponies and horses were of similar age and sex. In both groups more than 60% of

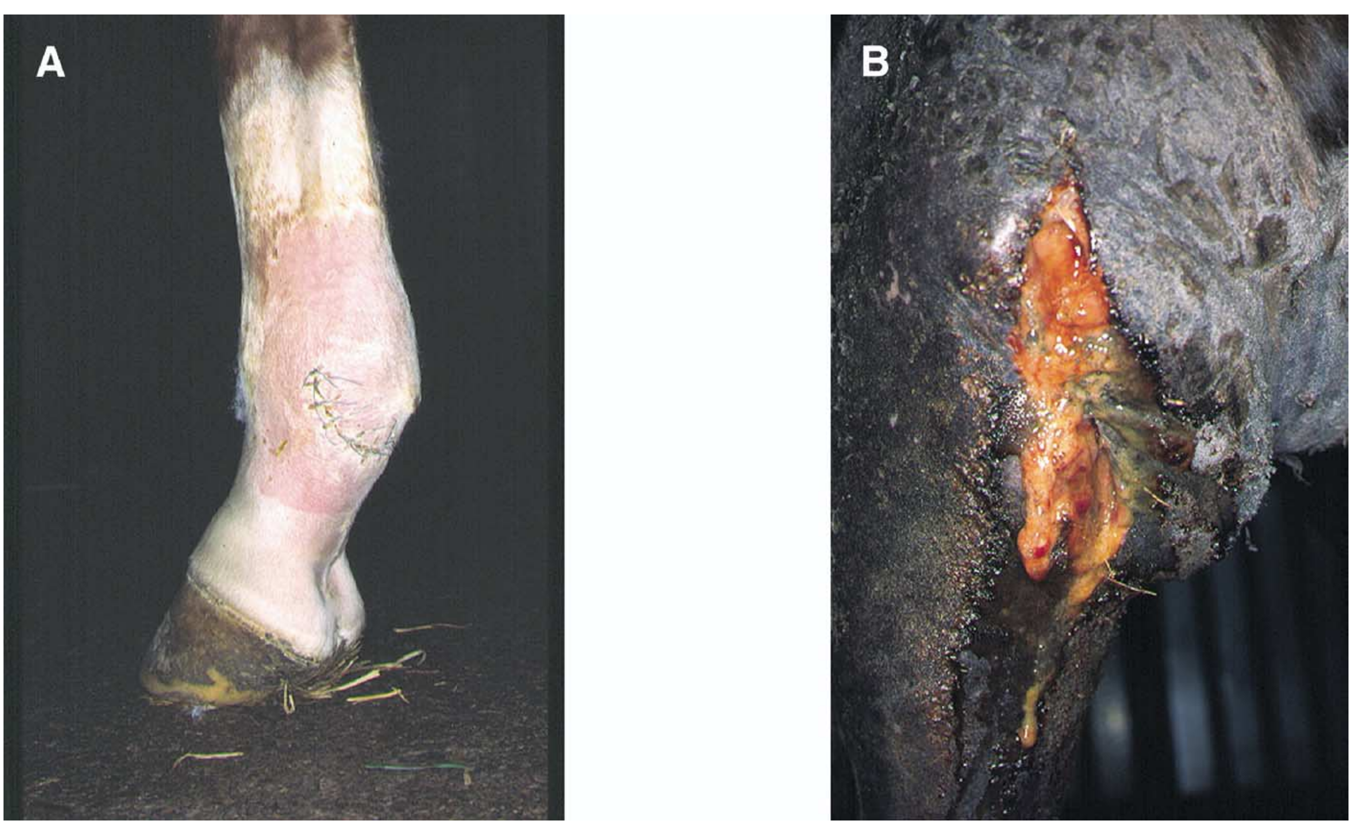


Figure 1 (A) Distal limb wound in a 4-year-old pony that healed successfully after primary closure, without dehiscence. (B) Dehiscence of a wound on the elbow as a result of wound infection.

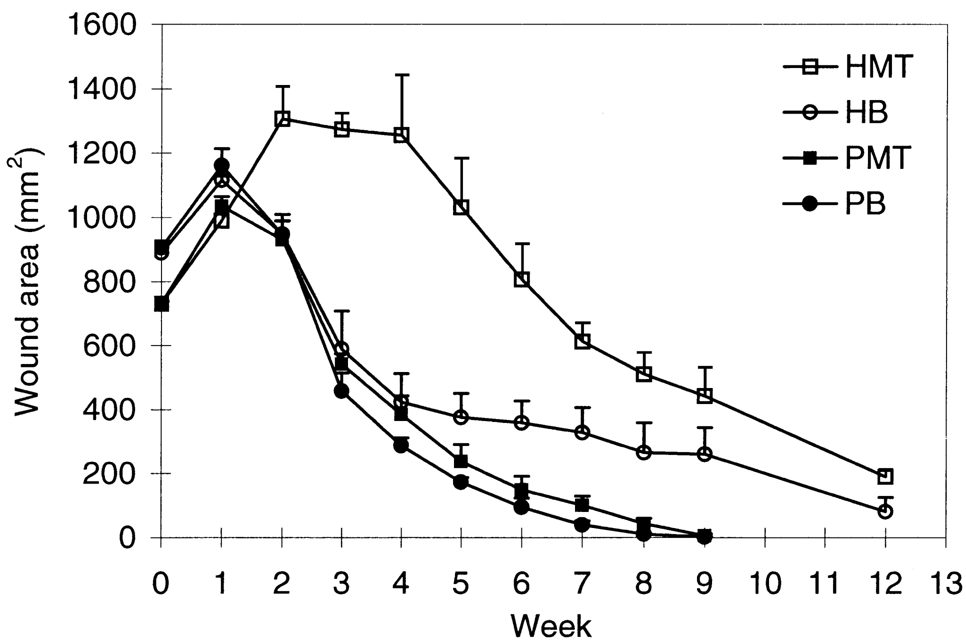


Figure 2 Wound area as a function of time (mean + s.e.m.). HMT = metatarsal wounds of the horses; HB = body wounds of the horses; PMT = metatarsal wounds of the ponies; PB = muscle wounds of the ponies (reprinted with permission[4]).

the wounds were located on the lower limbs (carpus, tarsus and distal to these sites). The wounds were comparable for location, duration and degree of contamination. However, in the ponies the wounds were generally deeper, with significantly more ruptured extensor tendons and more cases with a damaged periostium and exposed bone. Primary closure was attempted in approximately two-thirds of both ponies and horses. The closure was attempted more often in ponies while they were standing. Management after surgical treatment differed between horses and ponies: antibiotics and NSAIDs were given significantly less often to ponies, with no differences in the period of administration and choice of medication. Bandaging techniques and the frequency of application of a rigid cast were comparable for both groups. Successful primary closure was defined as complete healing by primary intention without any degree of dehiscence (Fig. 1). The study revealed that primary closure was significantly more often successful in ponies than in horses, and bone sequestra were formed significantly less often in ponies (Table 1). These findings suggest that wound infection affected healing less in ponies even though the conditions were less favorable. Ponies had a greater chance of a heavier bacterial challenge than horses by having deeper wounds, less thorough wound debridement in the standing position, and receiving antibiotics less often. Wound infection occurs when the level of bacterial contamination exceeds the capacity of the local tissue defenses. The local defense against the invasion of bacteria is determined by the inflammatory response.[9,10] Therefore, the results of this retrospective study suggest that the inflammatory response is more effective in ponies than in horses.

Second Intention Healing

Second-intention healing is a lengthy process, which often cannot be entirely controlled.[1] Historically, research on second-intention healing in horses focused on superficial full thickness skin wounds, which are hardly representative of wounds commonly seen in clinical practice. In the 1980s and 1990s observations from some studies posed the question whether ponies would heal faster without the formation of exuberant granulation tissue, as seen in horses.[11-13] However, none of these studies were specifically set up to investigate differences in wound healing between horses and ponies. As such it was proposed that these differences may provide important information about the basic biology of healing within the equine species. Research was performed in horses and ponies using standardized deep excisional wounds on the metatarsi and hind-quarters. The wounds exposed the bones on the metatarsi and had a depth of 18 mm on the hindquarters. This research confirmed differences in second-intention wound healing between horses and ponies: ponies healed significantly faster than horses (Fig. 2).[4,5] The following studies showed that these differences could be explained by differences in leukocyte-function.[14-16]

The wound healing process can be divided into several overlapping phases representing the events occurring during healing, eg, the inflammatory phase, formation of granulation tissue, wound contraction and epithelialization. Remarkable differences in these phases between horses and ponies are related to the speed and efficiency of healing.[4,5] The following discussion will relate to the aforementioned retrospective study.

Inflammatory Phase

During the inflammatory phase platelets, polymorphonuclear leukocytes (PMNs) and macrophages migrate to the wound site. The latter two cell types clear the wound of contaminating bacteria and nonviable tissue. Macrophages additionally release a plethora of biologically active substances, which are essential for the recruitment of more inflammatory and mesenchymal cells and start up the healing process.[10]

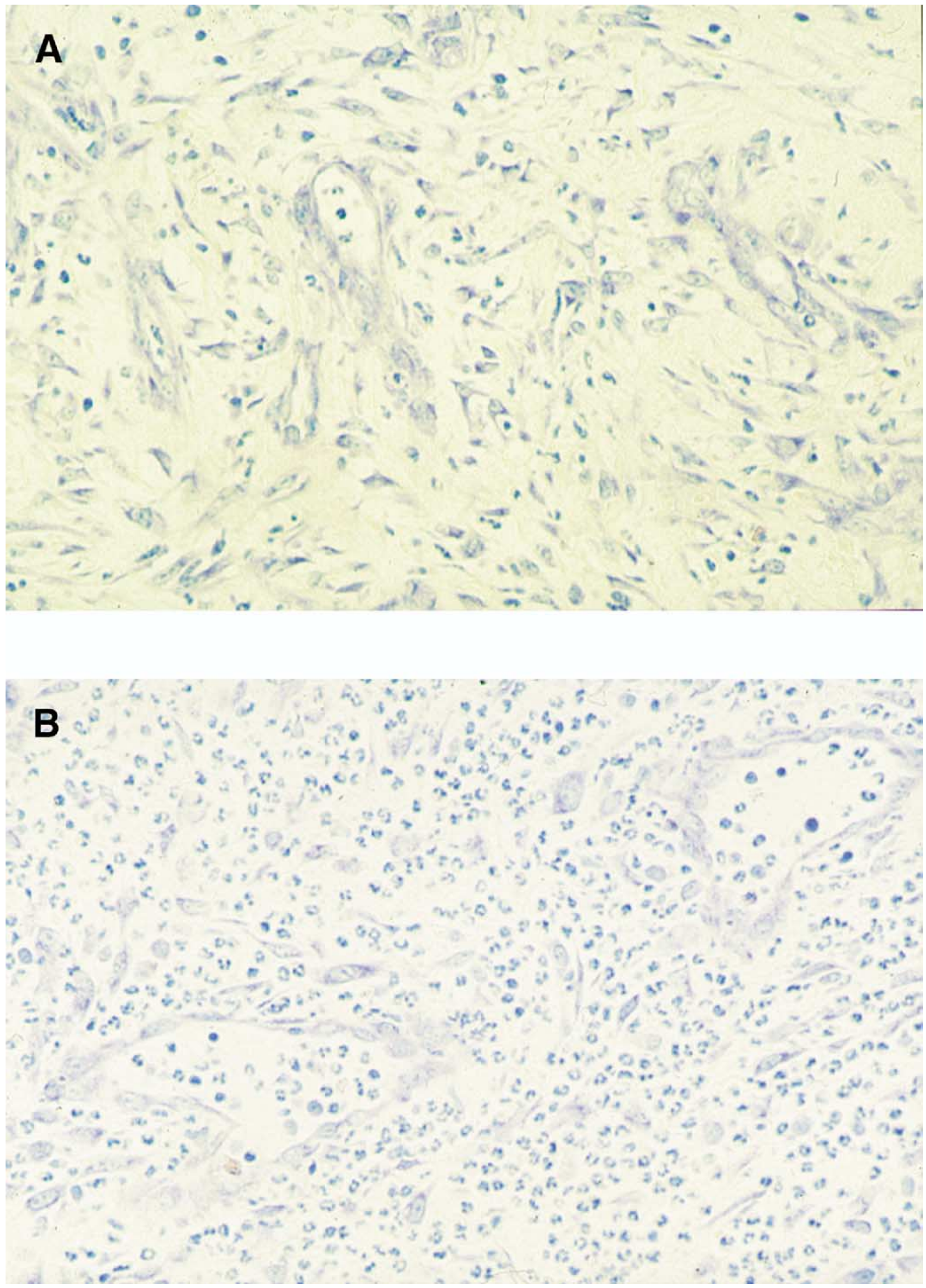


Figure 3 Histological appearance of the superficial layer of the granulation tissue of a horse wound (A) and a pony wound (B) after 1 week of healing. The initial influx of leukocytes had been faster in ponies than in horses.

In ponies, inflammation was seen earlier and a healthy granulation bed developed more rapidly, whereas in horses the granulation tissue remained irregular and purulent for longer with persistent fibrin depositions.[4,5] The initial influx of leukocytes in the wounds was faster in ponies than in horses, resulting in a higher number of PMNs during the first 3 weeks of healing in ponies (Fig. 3).[5] The PMNs subsequently disappeared rapidly in these wounds. In the horses, the influx was slower and the initial number of PMNs was lower, but thereafter the number remained persistently elevated (Fig. 3).[5] Further research showed that leukocytes of ponies produced more reactive oxygen species, which are necessary for bacterial killing. They also produced higher levels of other inflammatory mediators (TNFα, IL-1, chemo-attractants, TGF-β),[15,16] which are essential for the reinforcement of the inflammatory response, for the induction of formation of granulation tissue and for wound contraction.

In other words, the inflammatory response in ponies is initially stronger and of shorter duration. In contrast, the inflammatory response in horses is initially weak but then protracted. The course of the inflammatory response in ponies appears to be more efficient for the wound healing process.

Formation of Granulation Tissue

Fibroblasts, endothelial cells and macrophages move into the wound space as a unit and are dependent on each

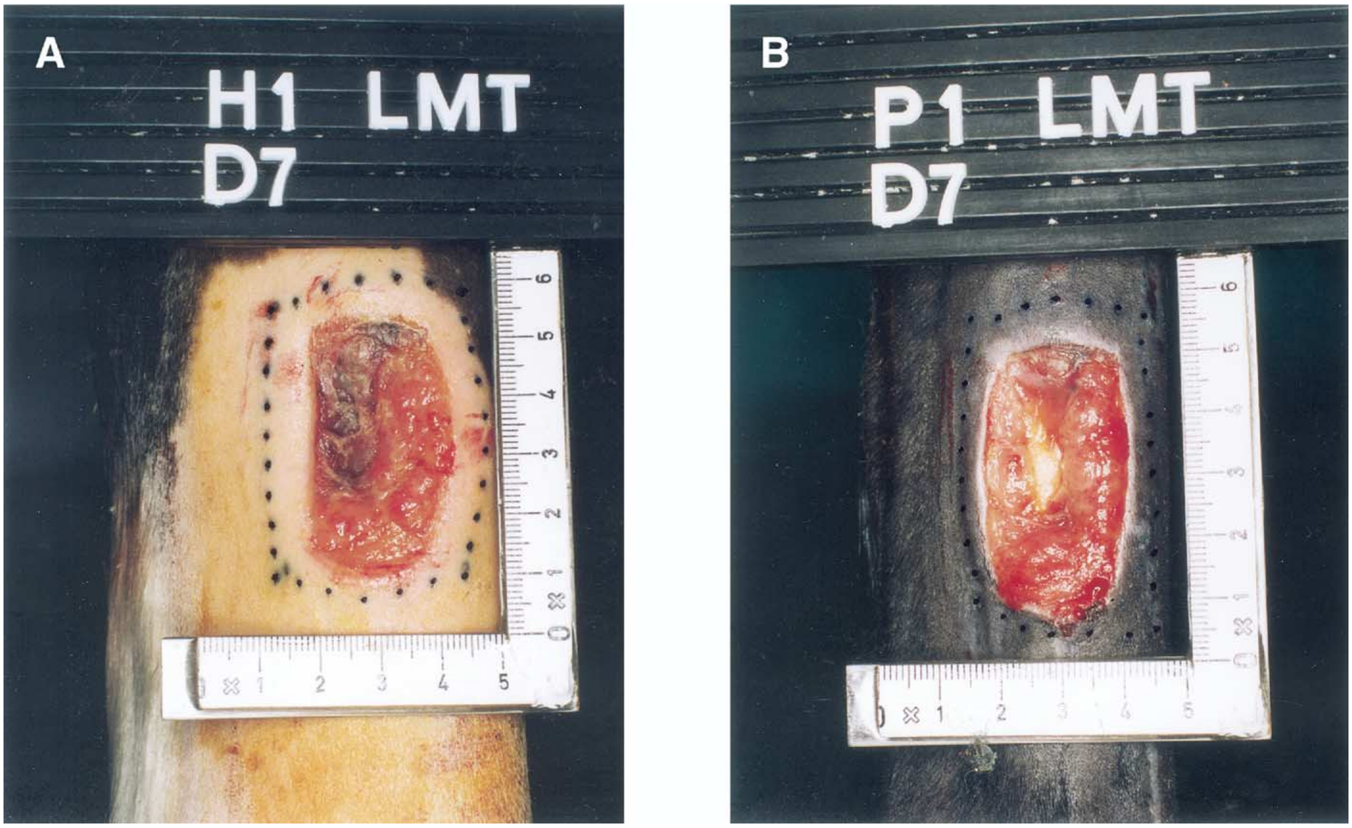


Figure 4 (A) The formation of granulation tissue in the horses was fast. After 1 week, the exposed metatarsal bone was completely covered with granulation tissue. (B) In contrast, the exposed bone in the ponies was still visible, and this lasted nearly 3 weeks.

other.[9] Macrophages are still believed to provide a continuing source of cytokines and growth factors necessary for the stimulation of fibroplasia and angiogenesis. Fibroblasts also are responsible for constructing a new extracellular matrix (ECM) needed to support cell ingrowth, and blood vessels transport oxygen and nutrients necessary to sustain cell metabolism.[17] Fibroblasts use the fibrin clot as a provisional matrix and rapidly replace it with a new loose ECM consisting of glycoproteins (fibronectin and laminin), proteoglycans (hyaluronic acid) and collagens (initially mainly type III, later type I).[18] Granulation tissue fills in the wound gap, and is necessary for wound contraction and for the migration of epithelium.

In the horses, the exposed metatarsal bones were completely covered with granulation tissue within one week, whereas complete coverage of the bones took nearly 3 weeks in ponies[4] (Fig. 4). After 2 weeks of healing, the granulation tissue of all wounds of both horses and ponies protruded somewhat above the level of the surrounding skin. At week 3, the limb wounds of the horses showed exuberant granulation tissue at both distal and medial wound margins, whereas in the limb wounds of the ponies this was only seen distally (Fig. 5). Also the wounds on the hindquarters had formed exuberant granulation tissue at all wound margins. After the wounds were left uncovered, exuberant granulation tissue disappeared spontaneously during the following week in most wounds, except the limb wounds of the horses, where the exuberant granulation tissue had to be trimmed.[4] The granulation tissue in the ponies became regular significantly sooner and it was pink and glistening significantly earlier than that seen in the horses. The tissue in the horses showed grooves and clefts for a much longer period and were purulent up to week 5 after the creation of the wound (Fig. 6). Histology showed that the proliferation of the horse fibroblasts continued, even after the wound had been completely filled with granulation tissue, whereas the pony fibroblasts ceased proliferation when the wound was filled in. Besides, the appearance of the granulation tissue was disorganized in the horses compared with the regular organization seen in ponies.[5]

Accordingly, the formation of granulation tissue in horses appears to be excessively fast, not only compared with other species, as was found in the past,[19] but also compared with ponies.[4] The fast formation and the persistent proliferation probably result in the formation of exuberant granulation tissue.[4,5]

Wound Contraction

Wound contraction is caused by the action of differentiated fibroblasts (myofibroblasts) in the granulation tissue, which contain filaments of smooth muscle actin. Contraction of these fibroblasts makes the wound margins move toward the center of the wound.[17,20]

Wound contraction started sooner in ponies than in horses and it was significantly more pronounced in ponies (Fig. 7). Additionally, it was significantly more pronounced in body wounds compared with the limb wounds. As a result, second-intention wound healing was significantly faster in ponies than in horses, and significantly faster in body wounds than in metatarsal wounds.[4] Histology showed that myofi-

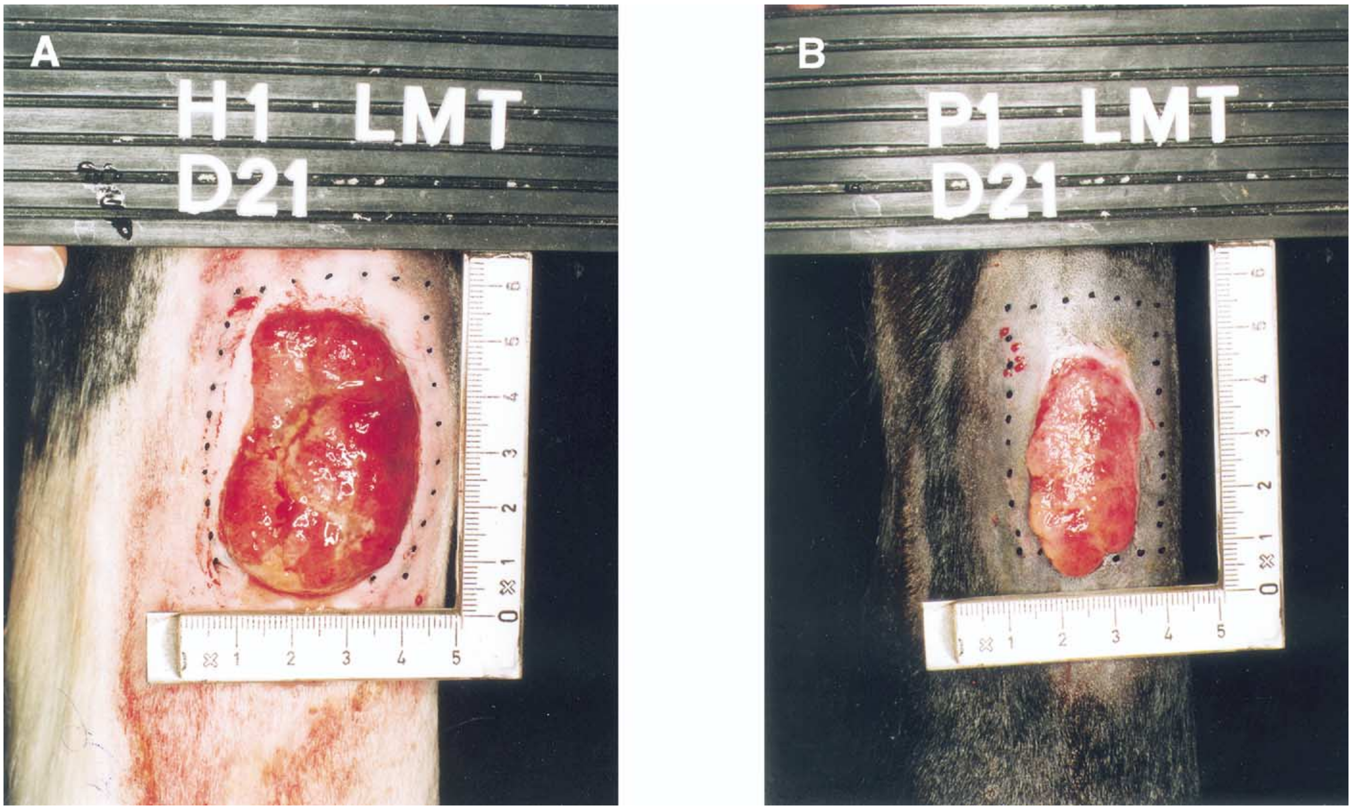


Figure 5 (A) After 3 weeks, the limb wounds of the horses showed more exuberant granulation tissue at both distal and medial wound margins. (B) The limb wounds of the ponies showed less exuberant granulation tissue only at the distal wound margin.

broblasts were more organized in the wounds of the ponies: the myofibroblasts in the newly formed granulation tissue were transformed into a regularly organized pattern within 2 weeks, in which the cells were orientated perpendicular to the vessels and parallel to the wound surface. This appears to be a more favorable condition for wound contraction to occur. In the horses, myofibroblast organization took much longer. No differences were found in the number of fibroblasts, the amounts of smooth muscle actin and collagen.[5] Further research was performed to investigate whether the differences in wound contraction between horses and ponies were caused by differences in the inherent contraction capacity of fibroblasts or the local environment of the fibroblasts. It was found that no differences existed in the inherent contraction capacity of fibroblasts from ponies and horses in vitro.[14] However, the level of Transforming Growth Factor β, the most important instigator of wound contraction, was significantly higher in the granulation tissue of pony wounds compared with horse wounds.[15]

In summary, the greater contribution of wound contraction to wound closure in ponies compared with horses results in a faster second-intention wound healing process in ponies. The differences in wound contraction are not caused by the contractile capacity of the fibroblasts but by mediators in the granulation tissue, such as TGF-β. Wound contraction appears to be an important mechanism of wound closure in the equine species because it occurs relatively early in the healing process and results in a fast closure of the wound by full thickness skin. Consequently, wound contraction determines largely the speed of second-intention wound healing and the final cosmetic appearance of the scar.

Epithelialization

Epithelialization occurs during the final phase of wound closure and is a very slow process (1 mm/10 days at the most in limb wounds of horses).[7] Although macroscopically it can only be observed from about 2 weeks after wounding, epithelialization starts a few hours after trauma with the migration of keratinocytes. Proliferation occurs after about 2 days, evoked by the secretion of many cytokines and growth factors by fibroblasts, inflammatory cells and by the keratinocytes themselves.[18,21] Epithelialization is impaired by fibrin remnants of the clot in the wound bed, chronic inflammation and exuberant granulation tissue.[22] Newly formed epithelium lacks skin adnexa and is thin and fragile because it has few epidermal projections[2] and this part of the wound remains visible as a superficial scar.

The mitotic activity of the epithelial cells was similar for horses and ponies during the first weeks of healing. However, the activity in all groups was temporarily reduced in week 3, when exuberant granulation tissue was present.[5] Thereafter, epithelialization became different for ponies and horses, limb and body wounds. An inverse relation between the epithelialized area and wound contraction developed: wounds demonstrating more wound contraction, showed less epithelialization. On the other hand, more epithelialization was seen when limited wound contraction occurred such as in the limb wounds of horses (Fig. 7). In these wounds epithelialization was particularly fast and from 6 weeks onwards sig-

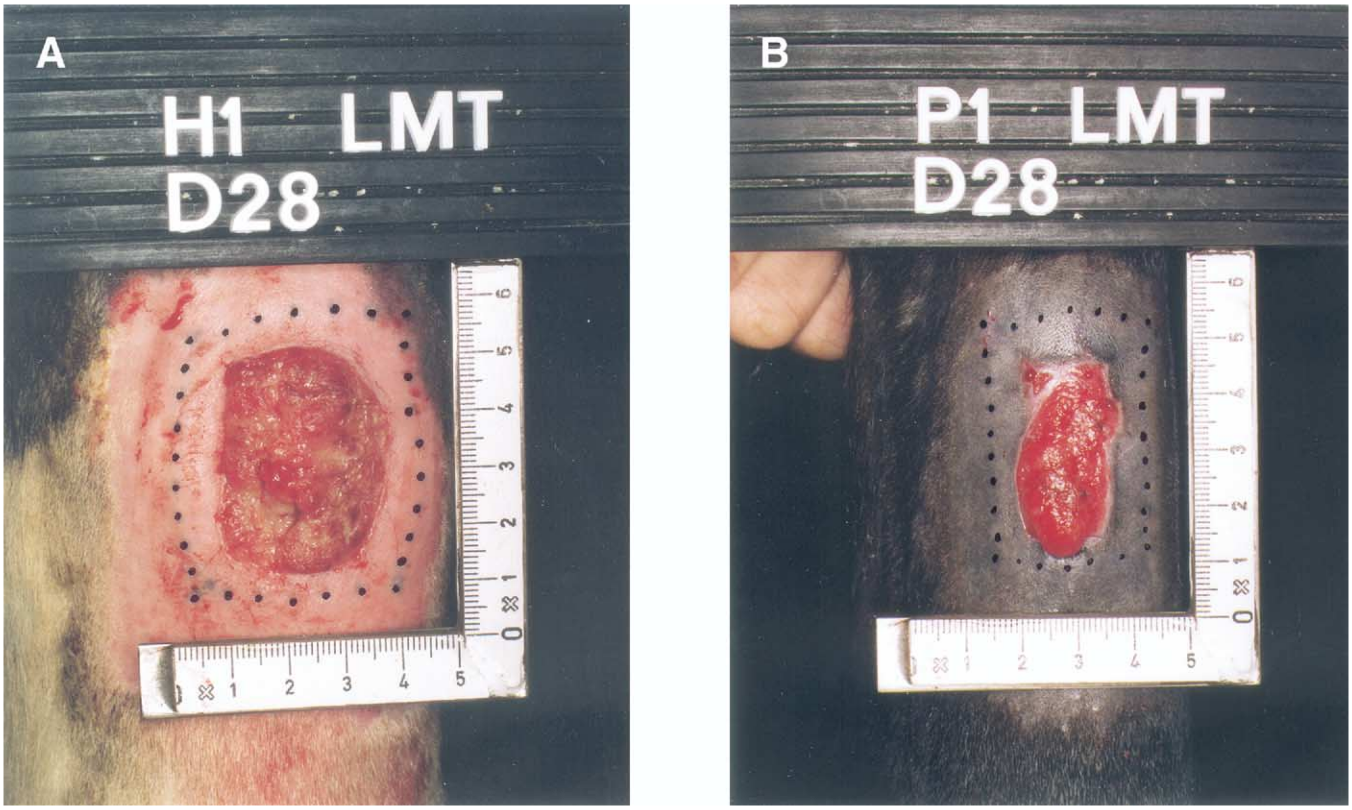


Figure 6 (A) The granulation tissue in the horses showed grooves, clefts and a purulence after 4 weeks, whereas (B) the tissue in the ponies was regular, pink and glistening sooner.

nificantly faster compared with all other wounds.[4] Finally, these wounds had the largest area of newly formed inferior epithelium and the most pronounced scars (Fig. 8).

In other words, epithelialization is slower when wound contraction is more rapid, as seen in ponies. This may be the result of the decrease in length of the wound margins by wound contraction from which epithelialization occurs. The effect of faster epithelialization on the speed of wound healing is limited because the process is inherently slow. When epithelialization is the primary mode of wound closure, this results in more extensive scars. The mitotic activity of epithelial cells is negatively influenced by the presence of exuberant granulation tissue and/or factors inducing exuberant granulation tissue.

Clinical Application of Research Results

Primary Intention Healing

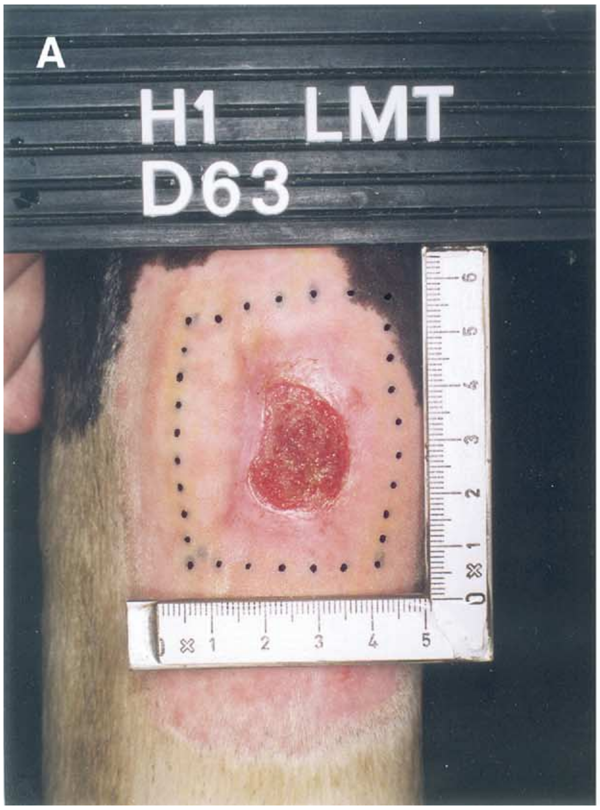
A retrospective study showed that ponies healed more favorable than horses after primary closure of traumatic wounds, although conditions were less favorable.[6] This means that the prognosis of traumatic wounds is better in ponies than in horses and expected costs of treatment are lower. In cases in which a pony-owner maybe reluctant to treat because of the costs in relation to the relatively low economic value of the animal, the better prognosis may justify treatment.

The results of primary closure show an important role of wound infection as a detrimental factor in the process of healing, and the important role of the inflammatory response in local defense. As yet, there are no proven ways to stimulate the inflammatory response to improve the local defenses; thus prevention of wound infection is of paramount importance. Therefore, the number of contaminating bacteria should be reduced, and infiltration and proliferation prevented.

Bacterial numbers can be reduced by low pressure (10-14 PSI) irrigation and thorough surgical debridement of the wound. This may even be more important than previously assumed. As thorough irrigation and debridement are more difficult to achieve in the standing animal, general anesthesia is preferred, especially when treating extensive limb wounds. Although primary closure in the standing animal may be seen as a physical challenge by the attending veterinarian, it is probably only warranted in very fresh and clean wounds. The debridement of exposed cortical bone also seems essential in prevention of infection and subsequent formation of a bone sequestrum.

Infiltration and proliferation of bacteria can be prevented by proper antimicrobial prophylaxis. Broad-spectrum antibiotics should always be given to horses and ponies with extensive traumatic wounds particularly those that expose bone. The intravenous route is recommended to ensure immediate high tissue levels. The application of the regional perfusion techniques[23] can be used in conjunction with the systemic administration of broad spectrum antibiotics. In the case of a referral, broad-spectrum antibiotics should be administered intravenously by the veterinarian who first attends the wounded horse.

The fact that the inflammatory response should initially be stimulated and not inhibited, implies that corticosteroids should not be used, and the routine use of NSAIDs is disput-



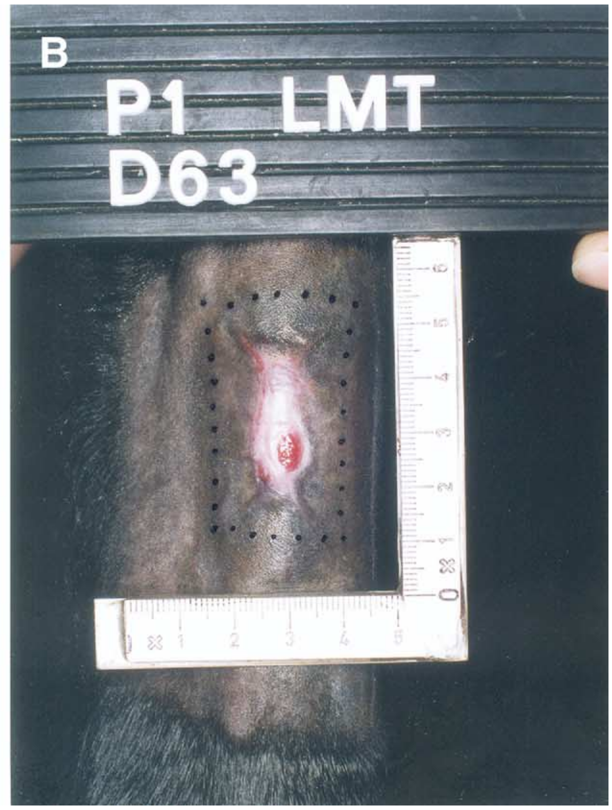


Figure 7 (A) After 9 weeks of healing the metatarsal wounds of the horses had decreased in size. The tattoos close to the original wound margins show that only minimal wound contraction occurred but pronounced epithelialization is visible. (B) Wound closure in the metatarsal wounds of the ponies was to a large extent caused by wound contraction, whereas the epithelialization was limited.

able. Adverse effects of NSAIDs have been reported on the migration of leukocytes, infection rate and on the healing of wounds.[24-26] NSAIDs may therefore increase the likelihood of wound infection. However, the use of NSAIDs may be inevitable in cases of (expected) severe lameness or abundant swelling that may compromise local circulation. In these selected cases, NSAIDs are used, but at as low of dose as possible and only for a limited period. Additionally, other medications that have a negative influence on the inflammatory response, such as local anesthetics, should preferably not be applied as local infiltration into the tissue, but as a regional perineural block or line block distant from the wound.[1]

In conclusion, measures should be taken to reduce contamination and to prevent any negative effect on the inflammatory response.

Second Intention Healing

Inflammatory Phase

It has been proven experimentally that the influx of leukocytes in the wound is relatively slow in horses compared with ponies and that leukocytes of horses produce lower levels of inflammatory mediators.[5,16] As the inflammatory response is a prerequisite for starting up healing, the initial inflammatory response in horses should in fact be stimulated and not be inhibited. Therefore as stated previously, the use of corticosteroids is not advisable and NSAIDs are questionable during the first phase of second-intention wound healing. Agents, which are toxic to leukocytes, such as some disinfectants, should be avoided. Additionally, wet bandages and hydrotherapy with cold water, used to "stimulate" the inflammatory phase, can be detrimental as they transiently decrease local tissue temperature and consequently cause vasoconstriction. A decrease in temperature slows biological processes and the ensuing vasoconstriction limits the supply of leukocytes, nutrients and oxygen. On the other hand, factors that increase inflammation, such as certain interactive dressing and topical agents, will stimulate healing.[27] This has been proven experimentally for the product Solcoseryl® (Solco Basle Ltd, Birsfelden, Switzerland).[28] A gel containing activated platelets (Lacerum® BeluMedX, Little Rock, AK) may also be expected to stimulate inflammation,[29] as well as alginate dressings, acemannan-containing hydrogel (Carravet Wound Dressing®, Veterinary Products Laboratories, Phoenix, AZ), Iodosorb® (Smith & Nephew, Hull, UK) dressings, honey and sugar. These products have the potential to activate macrophages but are not specifically tested in horses. Bandages in themselves speed up the biological processes during this phase by increasing local temperature and the availability of oxygen by causing a shift of the hemoglobin dissociation curve. Independently whether a wound can be sutured or not, surgical debridement is advisable when necrosis, exposed cortical bone or frayed tendons are present in a wound of a horse, because cellular debridement by the inflammatory response in horses is slow. After debridement, it is advisable to bandage the wound with interactive dressings or topical gels. Unfortunately, we are not yet able to stimulate the initial inflammatory response in a more specific

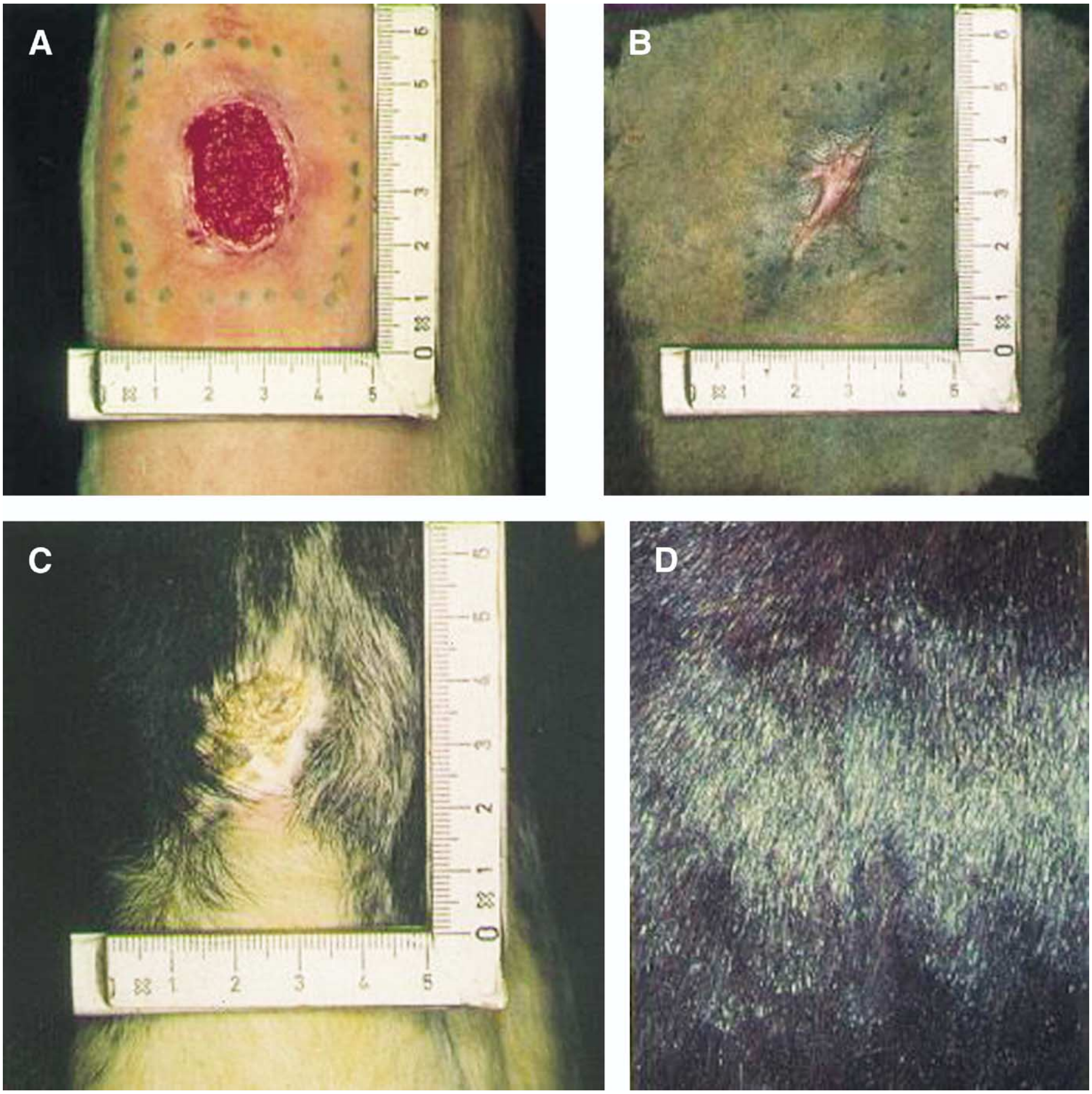


Figure 8 Metatarsal wound of a horse, after 9 weeks of healing (A) and 1.5 years later (C), and a body wound of a pony after 9 weeks (B) and 1.5 years (D).The limb wounds in horses closed mainly by epithelialization and an unsightly scar was present after complete healing. The body wounds of the ponies closed mainly by wound contraction leaving no visible scar behind.

way, although we know that this would be of benefit for the progress of wound healing in horses.

Formation of Granulation Tissue

Although the formation of granulation tissue in horses is fast, it is still desirable to stimulate the process until the wound has filled in. Many inflammatory mediators influence the formation of granulation tissue. However, the most important stimulus is the oxygen-gradient between the tissue and the wound surface. This is the way in which bandages and casts enhance the formation of granulation tissue[11]: by increasing the oxygen gradient and decreasing the pH. Therefore, initial stimulation of granulation tissue formation can be achieved just by bandaging the wound. Also a product such as Solcoseryl® and other occlusive dressings that promote moist wound healing stimulates this phase. However, stimulation should cease when the wound has filled in with granulation tissue.[28] If the formation of exuberant granulation tissue persists the cause should be diagnosed and eliminated. Reasons for persistent formation of granulation tissue include bone sequestrum formation, irritation by moving ends of tendons, foreign bodies, wound infection or chronic inflammation. It has been shown that horses develop a persistent, chronic inflammation during second-intention healing which can have an important effect on the occurrence of

exuberant granulation tissue. In case a special cause cannot be diagnosed, chronic inflammation can be expected to play a role in causing exuberant granulation tissue. In those cases, the chance of formation of exuberant granulation tissue decreases when surface contaminants and chronic inflammation are limited through proper treatment of the wound. In some cases the use of antiseptic wound dressings (eg, Kerlix® A.M.D. gauze Kendall, Mansfield, MA) or the local application of antimicrobials for a limited period of 1 or 2 weeks may be helpful to decrease surface contaminants which attract leukocytes and stimulate chronic inflammation. Limited use of local corticosteroids may also be helpful. Generally one application at the first evidence of exuberant granulation tissue is all that is needed. Such treatments are not only helpful in this phase, but will also stimulate the phases of wound contraction and epithelialization. Excision is another option for treatment[11] and has to be done as soon as possible, because exuberant granulation tissue inhibits wound contraction and epithelial migration and mitosis. When proliferation of granulation tissue is persistent, the bandages can be left off temporarily to decrease the stimulus for further proliferation.

Wound Contraction

Since wound contraction determines the speed of second-intention healing and the final cosmetic result it needs to be stimulated.[4] The differences in wound contraction between horses and ponies appear not to be caused by the contraction capacity of fibroblasts, but by local tissue factors.[14] It is known that wound contraction is stimulated by Transforming Growth Factor-β (TGF-β),[30] but inhibited by many inflammatory mediators,[31] which are abundant during chronic inflammation. The low initial production of TGF-β and the frequent occurrence of chronic inflammation[4,5,15] can therefore explain the limited contribution of contraction to wound closure in limb wounds of horses. In this respect, it could be expected that the application of TGF-β to wounds in horses would stimulate wound contraction, however this was not the case in an experimental study.[32] It was conjectured that the application form of TGF-β or schedule of application was not optimal. Chronic inflammation should be prevented or inhibited, which means that stimuli causing a chronic inflammatory response should be eliminated. Therefore, the wound must be protected from environmental micro-organisms and foreign material. This can be achieved by covering the wound surface with inert semiocclusive dressings. Further, the number of bacteria on the wound surface has to be controlled, as they are strongly chemo-attractive to leukocytes. In some cases, it is necessary to apply local antibacterial therapy for a short term, but care should be taken that the vehicle used does not induce inflammation. Systemic antibiotics are less effective, because their effect in the most superficial layer of the granulation tissue is limited. Antiseptic dressings (Kerlix® A.M.D. Kendall, Mansfield, MA) or silver chloride-coated dressings (Silverlon®, Argentum, Lakemont, GA) may have a positive influence when used for a limited period to suppress superficial contamination. Sometimes, chronic inflammation will persist in which case the local use of corticosteroids may be considered. However, corticosteroids should be used infrequently and for short periods, as they not only inhibit the inflammatory response, but also other phases of wound healing. Unfortunately, specific medication is not (yet) available to stimulate this phase.

Epithelialization

Epithelialization is the slowest phase of the healing process. The epithelialized part of the wound remains visible as a superficial scar. The conditions for optimum epithelialization include a regular, healthy bed of granulation tissue that does not protrude, and a moist environment. This phase is inhibited by exuberant granulation tissue and toxic products produced by leukocytes during chronic inflammation.[10] Granulation tissue should be excised as soon as the surface protrudes the wound margins. Not only the abundant tissue is removed but also surface contamination and excess of leukocytes, which are mainly present in the superficial layers of the granulation tissue. Additionally, the number of clefts decreases. This results in a healthier wound bed that is more favorable for contraction and epithelialization. As mentioned before, local antibacterial medication or antiseptic dressings may assist in reducing chronic inflammation and these are used preferably for a limited period of one or two weeks when necessary. A moist environment can be provided by semiocclusive dressings, however not by fully occlusive dressings, as these prolong healing time and stimulate the production of excess wound exudate and granulation tissue.[33] In large wounds, skin grafting will enhance the epithelialization phase dramatically by increasing the wound margins from which epithelialization takes place.

Conclusions

Knowledge of the phases of the second-intention wound healing is essential for the decision how to treat a certain wound. A maximal effect of treatment will be obtained if conditions for each phase are optimized. This means that the treatment regimen has to change during healing, and may even be different for various sites of the same wound. As no wound is the same, a simple time schedule cannot be given. The knowledge about differences in healing between horses and ponies resulted in the awareness that the acute inflammatory response should be encouraged, and not be suppressed under any circumstances. On the other hand, chronic inflammation has to be treated. Improving conditions for wound contraction has most effect on the speed of second intention healing and the final cosmetic result. Research is still required to develop new and better treatment methods in particular focusing on the inflammatory and contraction phase. The use of inflammatory mediators and growth factors is promising. It is very unlikely that any new successful method will consist of only one therapy or a single factor.

References

1. Caron JP: Management of superficial wounds, in: Auer JA, Stick JA (eds): Equine Surgery, vol 1 (ed 2). Philadelphia, PA, Saunders, 1999, pp 129-140
2. Jacobs KA, Leach DH, Fretz PB, et al: Comparative aspects of the healing of excisional wounds on the leg and body of horses. Vet Surg 13:83-90, 1984
3. Knottenbelt DC: Equine wound management: Are there significant differences in healing at different sites on the body? Vet Dermatol 8:273-290, 1997
4. Wilmink JM, Stolk PWT, van Weeren PR, et al: Differences in second-

intention wound healing between horses and ponies: Macroscopical aspects. Equine Vet J 31:53-60, 1999
5. Wilmink JM, van Weeren PR, Stolk PWT, et al: Differences in second-intention wound healing between horses and ponies: Histological aspects. Equine Vet J 31:61-67, 1999
6. Wilmink JM, van Herten J, van Weeren PR, et al: Study of primary-intention healing and sequester formation in horses compared to ponies. Equine Vet J 34:270-273, 2002
7. Stashak (ed): TSEquine Wound Management, vol 1 (ed 1). Philadelphia, PA, Lea and Febiger, 1991
8. Moens Y, Verschooten F, De Moor A, et al: Bone sequestration as a consequence of limb wounds in the horse. Vet Radiol 21:40-44, 1980
9. Clark RAF: Cutaneous tissue repair: Basic biologic considerations I. J Am Acad Dermatol 5:701-725, 1985
10. Cotran SC, Kumar V, Robbins SL: Cellular growth and differentiation: normal regulation and adaptations: Inflammation and repair, in Schoen FJ (ed): Robins Pathologic Basis of Disease, vol 1 (ed 5). Philadelphia, PA, Saunders, 1994, pp 35-92
11. Fretz PB, Martin GS, Jacobs KA, et al: Treatment of exuberant granulation tissue in the horse: Evaluation of four methods. Vet Surg 12:137-140, 1983
12. Bertone AL, Sullins KE, Stashak TS, et al: Effect of wound location and the use of topical collagen gel on exuberant granulation tissue formation and wound healing in the horse and pony. Am J Vet Res 46:1438-1444, 1985
13. Barber SM: Second intention wound healing in the horse: The effect of bandages and topical corticosteroids. Proc Am Assoc (Equine Pract) 35:107-116, 1990
14. Wilmink JM, Nederbragt H, van Weeren PR, et al: Differences in wound contraction between horses and ponies: the in vitro contraction capacity of fibroblasts. Equine Vet J 33:499-505, 2001
15. Van Den Boom R, Wilmink JM, O'Kane S, et al: Transforming growth factor-β levels during second intention healing are related to the different course of wound contraction in horses and ponies. Wound Rep Reg 10:188-194, 2002
16. Wilmink JM, van den Boom R, Veenman JN, et al: Differences in polymorphonucleocyte function and local inflammatory response as a possible cause for differences in wound healing efficiency between horses and ponies. Equine Vet J 35:561-569, 2003
17. Clark RAF: Biology of dermal repair. Dermatol Clin 11:647-666, 1993
18. Moulin V: Growth factors in skin wound healing. Eur J Cell Biol 68:1-7, 1995
19. Chvapil M, Pfister T, Escalada S, et al: Dynamics of the healing of skin wounds in the horse as compared with the rat. Exp Mol Pathol 30:349-359, 1979
20. Darby I, Skalli O, Gabbiani G: α-Smooth muscle actin is transiently expressed by myofibroblasts during experimental wound healing. Lab Invest 63:21-29, 1990
21. Clark RAF: Basics of cutaneous wound repair. J Dermatol Surg Oncol 19:693-706, 1993
22. Stadelmann WK, Digenis AG, Tobin GR: Physiology and healing dynamics of chronic cutaneous wounds. Am J Surg 176:26-38, 1998
23. Bertone AL: Update on infectious arthritis in horses. Equine Vet Educ 11:143-152, 1999
24. Sedgwick AD, Lees P, Dawson J, et al: Cellular aspects of inflammation. Vet Rec 120:529-535, 1987
25. Proper SA, Fenske NA, Burnett SM, et al: Compromised wound repair caused by perioperative use of ibuprofen. J Am Acad Dermatol 18: 1173-1179, 1988
26. Kahn LH, Styrt BA: Necrotizing soft tissue infections reported with nonsteroidal antiinflammatory drugs. Ann Pharmacother 31:1034-1039, 1997
27. Chvapil M, Holubec H, Chvapil T: Inert wound dressing is not desirable. J Surg Res 51:245-252, 1991
28. Wilmink JM, Stolk PTW, van Weeren PR, et al: The effectiveness of the haemodialysate Solcoseryl® for second-intention healing in horses and ponies. J Vet Med 47:311-320, 2000
29. Carter CA, Jolly DG, Worden CE, et al: Platelet-rich plasma gel promotes differentiation and regeneration during equine wound healing. Exp Mol Pathol 74:244-255,2003
30. Montesano R, Orci L: Transforming growth factor β stimulates collagen-matrix contraction by fibroblasts: Implications for wound healing. Proc Natl Acad Sci U S A 85:4894-4897, 1988
31. Ehrlich HP, Wyler DJ: Fibroblast contraction of collagen lattices in vitro: Inhibition by chronic inflammatory cell mediators. J Cell Physiol 116:345-351, 1983
32. Steel CM, Robertson ID, Thomas J, et al: Effect of topical rh-TGF-β1 on second intention wound healing in horses. Aust Vet J 77:734-737, 1999
33. Howard RD, Stashak TS, Baxter GM: Evaluation of occlusive dressings for management of full-thickness excisional wounds on the distal portion of the limbs of horses. Am J Vet Res 54:2150-2154, 1993